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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/835,523	04/17/2001	Yong-Qian Wu	23754X	5679

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EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/835,523	WU ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40 and 48-51* is/are pending in the application.

4a) Of the above claim(s) *5,6,11-40 and 49-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-10 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6-23-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

Applicant's amendment of 01-07-05 has been fully considered. The amended claims have overcome part of the previous 112/2nd rejection (i.e., definition of R_1), they have not overcome the remaining previous 112/2nd rejection as well as the previous 112/1st rejection. Since no terminal disclaimer has been filed, the previous ODP rejection is still outstanding. Therefore, all previous rejections are maintained herein.

Claims 5, 6, 11-40 and 49-51 have been withdrawn from consideration as being drawn to the non-elected subject matter.

Claims 41-47 have been cancelled.

Claims 1-4, 7-10 and 48 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

1. **Indefiniteness issues:**

Claims 1-4, 7-10 and 48 remain rejected under 35 U.S.C. 112, second paragraph for reasons stated previously, and the following:

Applicant's argument has not overcome the 112/2nd rejection on the limitations of "ester or solvate thereof", "carbocycle", "heteroaryl", and "heterocycle", "thiocarbonyl", "carbonyl" as well as "affecting a neuronal activity".

Applicant has taken the position that the above limitations are broad, but not indefinite. However, said terms are not just broad, they are indefinite for the following reasons:

a. Formula I has R_1 which can be an ester group such as: $-COOR_3$, and phosphoester (e.g., $-PO_3(R_3)_2$). Thus, it is unclear if could have another ester group. R_2 and R_3 do not appear to be able to form an ester group. Therefore, the location of an 'ester thereof' is indeterminate which renders the claim indefinite as well.

b. The term "carbocycle", "heteroaryl", "heterocycle" have indefinite metes and bounds because their definitions in the specification are open-ended. Particularly, "heteroaryl" and "heterocycle" seem to overlap in scope with the latter being broader. Likewise, the term "carbocycle" also has overlapping scope with the term "aryl". Therefore, reciting all these terms together in the definitions of R_2 and R_3 constitute an indefiniteness of 'broad & narrow limitations'. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131

USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

c. The limitations of "thiocarbonyl" and "carbonyl" have an open valency. Thus, it is not clear what the terminal group on said moieties is.

d. The limitation of "affecting a neuronal activity" is indefinite because it is not clear what "affecting" means. Does "affecting" mean "increasing" or "decreasing", "stimulating" or "inhibiting"? Because "affecting" can have many meanings, it renders method claims 7-10 indefinite.

2. **Enablement for "solvates"**:

Claims 1-4, 7-10 and 48 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's argument has not overcome the 112/1st rejection on the enablement for "solvates" of the compound of formula I. Applicant asserted that the claim for "solvates" is presumed enable by the disclosed process unless proven otherwise. However, the specification does not show how a "solvate" of the claimed compound can be made. The general process on columns 29 and 30 is directed to the synthesis of the compound of formula I, and not "esters" or "solvates thereof". There is no suggestion of what solvents to use to obtain a "solvate", nor is there suggestion on how a "solvate" can be isolated, crystallized, or if a polymorph is formed.

Such a process would definitely require undue experimentation because a "solvate" could be polymorphic which could alter solubility, stability as well as bioavailability.

3. **Enablement for method claims 7-10:**

Claims 7-10 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant asserted that a statement of "*manner and process of using the invention*" should be sufficient for the "how to use" requirement unless proven otherwise. However, in the instant case, it is not even clear what "affecting" means (see the above 112/2nd rejection).

a. The claims cover not only the treatment, but also the prevention of various neurological diseases including (without limitation): *trigeminal neuralgia; glossopharyngeal neuralgia; Bell's Palsy; myasthenia gravis; muscular dystrophy; amyotrophic lateral sclerosis; progressive muscular atrophy; herniated, ruptured or prolapsed inverterbrate disk syndromes; cervical spondylosis; plexus disorders; thoracic outlet destruction syndromes; peripheral neuropathy; Guillain-Barre syndrome; Alzheimer's disease; Huntington's disease; and Parkinson's disease, etc.*

b. The above neuronal diseases have different manifestation. For example, muscular dystrophy and myasthenia gravis affect the muscle whereas Alzheimer's and Huntington's disease affect the brain. Many of said diseases come from peripheral

nervous system while others come from central nervous system. Therefore, using the claimed compound to treat a disease of peripheral nervous system could adversely affect the central nervous system as well.

c. The specification does not provide a correlation between treating or preventing the above diseases with the biological activity of the claimed compounds.

d. As for the state of the art, compounds of pyrazolidine ring appear to have the activity of pesticides (see **Jacobson** US 5,109,014 & US 5,256,670) while compounds of pyrazine ring appear to have the activity of collagenase inhibitor (**Sugimura et. al.** US 5,643,908). Therefore, the state of the art does not support the instant method claims.

e. Given the unpredictability of the pharmaceutical art, (particularly, the treatment of neuronal diseases), and the limited guidance provided, the skilled clinician would have to carry out undue experimentation to treat or prevent neuronal diseases as recited in claims 7-10.

Double Patenting

4. Claims 1-4, 7-10 and 48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,417,189. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons stated in the previous action.

No pending claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (10:00-6:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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3-20-05

Tamthom N. Truong
Examiner
Art Unit 1624

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